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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,755	03/24/2004	Paul D. Robbins	072396.0263	4352

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BAKER BOTTS L.L.P.
30 ROCKEFELLER PLAZA
44TH FLOOR
NEW YORK, NY 10112-4498

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DLNYDOCKET@BAKERBOTTS.COM

Office Action Summary	Application No.	Applicant(s)	
	10/807,755	ROBBINS ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,22 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *6-13 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,14,15,17-19, 22 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19, 22 and 30-32 are pending in this application. Claims 6-13 and 16 are withdrawn from consideration for being drawn to non-elected subject matter but should the generic claims be found allowable, applicants will be entitled to consideration of claims to additional species, which depend from or otherwise require all limitations of an allowable generic claim.

Claim Objections

Claims 1 and 30-32 is objected to because of the following informalities: Claim 1 appears to be drawn to a vector constructed from complementary pairs of oligonucleotides that overlap such that the regions of overlap anneal to form the final vector. However, the recitation "vector comprising one or more pairs of chemically-synthesized, overlapping complementary oligonucleotides" in claim 1 does not reflect this relationship accurately as it is unclear what is the pair and what is overlapping. It would be clearer to recite -- vector constructed from one or more overlapping pairs of complementary chemically-synthesized oligonucleotides--. However, it is noted that the art need not read on a vector prepared from overlapping pairs of complementary oligonucleotides so long as the art product is the same or similar to the final product.

Furthermore, claims 30-32 recite that the one or more pairs of overlapping are annealed to form the oligonucleotide and hence are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper

dependent form, or rewrite the claim(s) in independent form. The vector of claim 1 already comprises these oligos annealed and ligated.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The instant claim is drawn to a DNA vector comprising a RNA promoter, a transcriptional terminator and a region to be transcribed wherein the vector is less than or equal to about 135 base pairs. The vector is designed to express ss or ds RNA molecules that may function as ribozymes or antisense siRNA. Specifically, applicants teach RNA polymerase

promoters wherein the promoters are selected from the human H1 polymerase II promoter, human type 1 polymerase III promoter, human type 2 polymerase III promoter, human type 3 polymerase III promoter, human pol II promoter, adenovirus major late promoter, and tissue-specific or inducible variants thereof. As well applicants claim regions to be transcribed wherein the sequences can be SEQ ID NO: 16, which is 82 nucleotides.

Applicants argue that the specification teaches methods of reducing vector size in examples 6, 7, 9 and 15. These sections describe vectors that are about 130 base pairs in length. These examples require manipulations of the promoter and/or sequences encoding the RNA molecule. In the case of H1 polIII promoter, the vector would require either full length H1 promoter and less than an additional 35 nucleotides or truncated H1 promoter and less than an additional 65 nucleotides. In either case, the RNA molecule of SEQ ID NO:16 cannot be part of a vector less than 135 base pairs as SEQ ID NO:16 is 82 nucleotides. The invention has been assessed as it relates to the prior art, which does not teach that a vector can be generated, that is smaller then the single components that are required. As well, applicants do not provide the structural requirements of a vector less then 135 base pairs such that a person of skill in the art can identify those components that are not required of the disclosed vectors and that can still mediate expression of a region into an RNA molecule

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 14, 15, 30-32 are rejected under 35 U.S.C. 102(a) as being anticipated by McManus et al (RNA (2002), 8:842–850; see entire document).

McManus et al teach a vector comprising two DNA oligos containing H1 polymerase III sequence and an RNA sequence annealed to one another (see page 849, col 1, ¶ 1 and figure 6). The promoter is the H1-RNA promoter should be absent evidence to the contrary be the sequence set forth in SEQ ID NO:20 which is human H1 polymerase III and is 100 base pairs. As depicted in figure 1, these RNA sequences can be less than 35 base pairs. While figure 6 depicts the vector cloned into pCRII-TOPO, prior to its cloning, this DNA constitutes a vector in its own right. The vector as a product is the same regardless of how it is ligated and hence claims 30-32 denote the same vector as that described in claim 1.

Claims 1-5, 14, 15, 19, 30-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al (20040115815; see entire document).

Li et al teach a chemically synthesized vector comprising H1 polymerase III sequence and an RNA sequence as well as a terminator (see figure 5, ¶238, and claim 1 and 3). The promoter is the H1-RNA promoter should be absent evidence to the contrary be the sequence set forth in SEQ ID NO:20 which is human H1 polymerase III and is 100 base pairs. As depicted

in figure 1, the RNA sequences are less than 23 base pairs. The vector further comprises targeting ligands (see e.g. ¶ 238). The cassette is directly inserted into cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 14, 15, 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castanotto et al (RNA, 2002, Vol 8(11), pages 1454-1460; see entire document) in view of McManus et al (RNA (2002), 8:842–850; see entire document) or Li et al (20040115815; see entire document).

Applicants claim a dsDNA vector comprising a RNA promoter, a transcriptional terminator and a region to be transcribed wherein the vector is less than or equal to about 135 base pairs. The vector is designed to express ss or ds RNA molecules that may function as ribozymes or antisense siRNA.

Castanotto et al teach a cassette formed by annealing two primers comprising a RNA promoter as well as sequences to be expressed as siRNA molecules and a terminator (see figure 1). The RNA molecules are 21-23 nucleotides in length. The cassette is not further cloned (see e.g. page 1455, col 1, ¶ 1).

While the vector of Castanotto et al can be less than or equal to 135 base pairs, it is not clear what size the promoter is. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the U6 promoter taught by Castanotto et al with the H1 promoter taught by McManus et al or Li et al because Castanotto et al teach that it is within the ordinary skill of the art to express siRNA from a cassette under control of a RNE promoter and because McManus et al and Li et al teach that it is within the ordinary skill of the art to use an H1 promoter for such expression. As an initial point, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision Exparte Smith --USPD2d--., slip op. at 20, (BD. Pat. App. & Interfer. June 25, 2007). Only so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, the combination of Castanotto et al and McManus et al/Li et al demonstrates an attempt to use known techniques to improve similar constructs using skill that was available at the time of filing with well-established methods on well-characterized adenovirus. At the same time, one would have been motivated to do so in order to receive the expected benefit of using the H1 promoter in expression cassettes that do not require further cloning given the success documented using H1 in this instances as well as its compact nature. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Castanotto et al (RNA, 2002, Vol 8(11), pages 1454-1460; see entire document) in view of McManus et al (RNA (2002), 8:842–850; see entire document) or Li et al (20040115815; see entire document) as applied to claims 1-5, 14, 15, 30-32 above, and further in view of Kassavetis et al (EMBO J, 2001, Vol 20(11), pages 2823-2834; see entire document).

Applicants claim a dsDNA vector comprising a RNA promoter, a transcriptional terminator and a region to be transcribed wherein the vector is less than or equal to about 135 base pairs. The vector is designed to express ss or ds RNA molecules that may function as ribozymes or antisense siRNA and comprises a heteroduplex bubble.

Kassavetis et al teach that insertion of a heteroduplex bubble into a vector comprising an RNA polymerase promoter partially opens the promoter and bypass the requirements for B" protein or Brf protein in transcriptional activation (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the bubble taught by Kassavetis et al into the vector taught by Castanotto et al in view of McManus et al or Li et al because Castanotto et al in view of McManus et al or Li et al teach that it is within the ordinary skill of the art to express siRNA from an RNA polymerase promoter and because Kassavetis et al teach that it is within the ordinary skill of the art to use a heteroduplex bubble to improve such expression. One would have been motivated to do so in order to receive the expected benefit of improved expression of the siRNA. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Examiner
Art Unit 1633

/Maria B Marvich, PhD/
Examiner, Art Unit 1633